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RADIUM

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VOL. V SEPTEMBER, 1915 No. 6

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D. with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. V. SEPTEMBER, 1915 No. 6

A BRIEF OUTLINE OF THE STATUS OF RADIUM THERAPEUTICS*

By CURTIS F. BURNAM, M.D.

Fellow alumni, it is a great pleasure to join with you in this twenty-fifth anniversary celebration of The John Hopkins Medical School.

The limited time at my disposal makes somewhat difficult a clear presentation even of the barest outline of the ascertained facts and questions which arise in considering the status of radium as an agent for treating diseases. Therefore, you will, I trust, pardon any glaring omissions or obscure statements. Volumes could and have indeed already been written on this many-sided subject. I shall be satisfied if I awaken your interest and stimulate you to further investigation of the radium question.

So much that is exaggerated, so much that is unscientific, so much that is absurd have appeared in both the lay and professional press of this country, that it need excite no wonder that most of you are probably in doubt as to whether radium really belongs to the armamentarium of the physician or of the quack. Some of the best-known surgeons in America have publicly gone on record with statements that radium is without any value whatever; others more guarded have stated that it is of marked value in treating superficial cancers and skin diseases, adding that its rays are practically identical with those from an X-ray tube. These opinions might be neglected, as the authors have almost invariably had no experience with radium, except for the fact that their wide reputations give undue weight to their opinions, and bias many of our profession, who are misled into believing that such conclusions are the

*From the Johns Hopkins Hospital Bulletin, Vol. XXVI, No. 291, pp. 190-196, May, 1915. The Editors wish to acknowledge the kindness of the Editor of the Johns Hopkins Hospital Bulletin in loaning the cuts which are reproduced in this article.

fruits of careful and painstaking investigations. The attitude of European medical leaders stands in sharp contrast to this opposition in America; in Germany especially the radio-active substances have been eagerly welcomed and are being painstakingly tested out by the leaders of medical and surgical thought. Practically all of those who have used radium consider it an agent of great value, and some of the most eminent men, as Doederlein in Munich, have expressed enormous enthusiasm and hope for its possible accomplishments.

Although radium has been employed in treating cancer and other diseases for more than ten years, the acute interest in it and most of the now great medical literature in regard to it have been produced during the last three years. This long latent period seems to have been much more due to scarcity of material than to the failure of those using it to secure suggestive and interesting results. For a time the only source of radium was the pitchblende deposits in the Joachimsthal Valley in Bohemia. These mines were bought from private individuals and have been operated for several years by the Austrian Government. During the last three years radium has been produced in quantity from American, Austrialian, Portuguese pitchblende deposits and other minerals. In addition to the greatly increased radium production, the discovery of mesothorium by Hahn has led the Welsbach Company of Germany to produce a large amount of this substance, which has similar physical properties and is considerably cheaper than radium. The distribution of mesothorium to the medical clinics in Germany has led to very active investigations and many publications. You have but to refer to the journal, *Strahlentherapie,* now in its fifth volume, to appreciate the amount and the character of the work already accomplished.

In the United States the names of Howard A. Kelly, Robert Abbe and William Morton will always be associated with the development of radium therapeusis; they were the pioneers here and have consistently advocated its use amidst general discouragement.

My own experience has been gained through association with Dr. Kelly and extends back about eight years, when he purchased his first small amount of radium. Two years ago we added greatly to this original store and since then have continued to increase it, until to-day, and for some months we have been working with about one gram and a quarter of radium element. This is not a large amount although it relatively seems so. We have repeatedly used the entire amount for a period of 48 hours in treating a single case. At the Howard A. Kelly Hospital, where the work of Dr. Kelly, Dr. Robert Lewis and myself has been carried out, we have treated nearly 1300 cases up to the present time. Some of these are four or five years old, but most of them are of the last two years.

I should prefer for time's sake to omit all reference to the chemistry and physics of radium, but so completely does an intelligent comprehension of the medical uses of the material depend upon an elementary knowledge of its physical properties, that a brief explanation seems unavoidable.

Radium is a metallic element belonging to the strontium barium group. It readily forms salts with the mineral acids and is the leading member of the peculiar radio-active group of elements which are characterized by atomic instability. Radium itself is formed by atomic reduction from uranium. It loses a portion of its atom to become a gas called radium emanation, and this in turn is the mother, grandmother,

etc., of a series of solid elements. The so-called radium C, third in series from the emanation, is that member of the group which particularly concerns us, as it is from it that both the beta and gamma rays are derived. Radium emanation can be separated from radium as fast as it is formed. A given amount of radium is capable of producing a given amount of emanation. The emanation reaches a maximum and then disintegrates at the same rate that it is being formed. In about four days a given amount is reduced to one-half. If radium or radium emanation is sealed in a glass or a metal container it begins to produce radium C. The maximum amount of radium C is obtained in a radium preparation so placed in a glass tube in thirty days. The maximum amount from emanation is produced in three hours and thirty minutes. Radium C itself can be isolated, but has such a short life, only two or three hours total, that it cannot be effectually used in practical treatment.

The essential characteristic of the radio-active substances is the giving off of invisible rays. These rays must not be confused with the emanation, which is an element just as radium itself is. The rays have been divided according to their physical characteristics into three kinds: the alpha, the beta and the gamma.

The alpha ray is a positively charged atom of helium. It has a very small power of penetration, being completely stopped by a thin sheet of writing paper. It acts very powerfully towards inducing chemical change in both inorganic and organic matter brought in contact with it. The beta ray is a negatively charged electrical ion which has about the velocity of light and will easily penetrate several centimeters of living tissue. It has also a marked capacity for inducing chemical changes in organic matter subjected to it. The gamma ray is not particulate matter, but a vibration of ether similar to ordinary light and of the X-ray. It differs from them in being of much shorter wave length and of much greater penetration. It has power also, but to a lesser degree than the alpha and beta rays, to produce chemical change in organic matter exposed to it. When a radium salt is inclosed in a glass tube, alpha, beta and gamma rays are produced within the container. The alpha rays are held in the tube, while the beta and gamma rays penetrate its walls, and pass out into the surrounding medium in radial lines, thus making a sphere of radiation. When the glass tube is further surrounded by 2 mm. of lead, the hardest beta rays can no longer penetrate this envelope. It is possible, therefore, in medical treatments to use all three kinds of rays together, the beta and gamma rays together, or the gamma rays alone. It is impossible to use the alpha rays alone, and it is difficult to use the beta rays alone in anything except experimental work.

From the above it is evident that radium or one of its derivatives can be used in two essentially different ways: firstly, it can be taken into the body by mouth, hypodermically or intravenously as any other soluble drug; secondly, it can be applied from either outside or inside the body in sealed tubes or other containers in the same general way that an X-ray tube is employed.

The internal use of radium or of radium emanation, which being a gas can be readily taken up through the lungs, has been principally investigated in Germany, and offers an immense field for study. There seems no question but that certain forms of gout, rheumatism, chronic arthritis and neuralgia can be greatly helped by its use. It has a pro-

nounced effect upon the hemapoietic tissues, in small doses stimulating, and in large doses destroying them. Unquestionable improvements have followed its use in cases of pernicious anæmia, leukæmia and erythropolycythemia; likewise in certain patients suffering with high blood-pressure, a return to the normal with complete disappearance of subjective symptoms being frequently obtainable. Our own experiences with these perhaps properly called medical uses of radium, have been too limited to permit us to do more than to state that we have seen encouraging results in many of these conditions and that we are also favorably impressed with the reports from abroad as well as with personal interviews with nearly all the well-known investigators in this field. We believe that under the strictest diagnosis and general medical investigation, with the co-operation of an experienced radiophysicist, this form of using radium will prove a valuable adjunct to existing methods of treating disease, and that the cases suitable for it will be determined. At the present moment this is certainly not the case, for the greatest confusion obtains. The situation is comparable to what the salvarsan treatment of syphilis would be under conditions where there was no definite diagnosis possible, and where the doses of the salvarsan used varied from one one-hundredth to ten times the dose actually found efficacious to-day. Can the confusion be wondered at?

Taken internally, radium acts with all its rays on all parts of the body. When sealed in glass or metal containers and properly disposed, any part of the body can be subjected to gamma radiation, and many parts of the combined gamma and beta radiation. A given part of the body can be radiated either by placing the radium carrier on the outside or on the inside of it. It is this local radium action which has been the principal object of our investigations. Such applications of radium are for convenience sake called the surgical uses of radium.

The method of separating the gamma rays from the total rays has already been described. There are, however, two other important physical considerations that must be borne in mind: first. that as the rays are given off from a point in every direction, the intensity must of necessity vary inversely with the square of the distance; this is best exemplified by taking a tube of radium and placing it 1 mm. away from a surface to be treated, and then taking the same tube and placing it 1 inch away from the surface to be treated. In the first instance we will say that in one minute the surface immediately underneath the tube receives one unit of radiation. In the second case, to determine the amount of radiation it is necessary to square 25 mm., which is the number of millimeters in an inch. When this is done it evident that in one minute the skin immediately underneath the tube receives only one six hundred and twenty-fifth of a unit of radiation, or, expressed in another way, the tube at 1 inch would have to be left 625 minutes to obtain a unit dose on the surface. Sticking to our example, suppose the endeavor is made to radiate tissue 1 inch below the surface with the tube in the first place 1 mm. distant, the surface would receive 625 times the dose that the tissue to be radiated would receive. On the other hand, when the tube is 1 inch away from the surface, the surface dose is only four times as great as the dose 1 inch underneath the surface. By increasing the distance from the skin, the dose at 1 inch depth can be brought nearer and nearer to the dose given the surface. It is apparent, however, that with a given amount of radium the time must be greatly increased, or with a given time the amount of radium must be propor-

tionately increased. The second important factor is that the tissue of the body absorbs a definite amount of the ray, and this is in proportion to its penetration. With hard rays much greater penetration is obtainable than with soft. This is well recognized in X-ray work.

The ideal aim in radiation is to apply to all parts of the diseased area or volume to be treated as equal a radiation as possible. The radium must therefore be placed in such positions with reference to the field that this is obtainable. In radiating a given area of the body and reporting results, it is essential that the type of growth, its location, its exact volume, the general condition of the patient, the amount of radium, the duration of the application and the distribution of the radiation be all clearly stated. In surface and near surface applications filters should not be dense and should allow action of the beta as well as the gamma rays. Where deepseated regions are to be treated from the outside, owing to the absorption by the tissues of the beta rays, only gamma rays should be employed. For example, in treating skin diseases the radium is best applied in large, flat applicators directly on the surface, and in treating intra-thoracic growths, the applicator should be surrounded by at least 2 mm. of lead and placed at least 2 inches away from the skin. A deepseated growth may be radiated from a number of different skin portals, thus bringing the dose in the interior to any desired quantity without over-treating any one spot of the surface. In addition to this distance radiation evenness of radiation is securable in the following way:

Fine, capillary glass tubes are filled with radium emanation and these containers are placed in hollow needles. It is possible to insert a number of such needles at a uniform distance from each other into the tissues to be radiated. By this means it is possible to radiate a given volume, as for instance the floor of the mouth, the tongue and neck, with an approximately uniformly equal and easily determinable beta and gamma radiation. It can readily be seen that where applicable this method is much more economical than distance radiation. Great care, however, must be taken that the exposure is not so long or intense as to cause sloughs or other injuries. It is proper to say in this connection that as yet the elementary facts are just being worked out. It is not known, for example, whether a short intense or a prolonged feeble radiation is preferable. The determination of this one point, alone will demand a tremendous material most carefully studied, and there are many others.

It is often asked, how does radium act? More than one uninitiated pathologist has stated that it acts simply as a very efficient cautery. Nothing could be further from the actual fact. While it is true that very intense radiation applied for a long period brings about complete necrosis and sloughing of tissue, nevertheless such sloughs are extremely hard to control and lead to painful wounds. As a cautery, radium is much inferior to commoner agents. The general impression that the advocates of radiation hold is that the radiation has a selective, deleterious influence on all pathologic tissues, but does not harm normal tissues. I have been frequently asked why is it that the rays pick out only the pathologic cells and leave the healthy cells? As a matter of fact, there is a marked selective tendency in this direction. It can be assumed that radiation deleteriously affects all living tissue, but that under this injurious influence the normal tissues are preserved because the fluids and the protective agencies of the body are all constructed to help the

normal tissues, and that the pathologic tissues disappear because, weakened by the radiation they are unable to withstand the normal protective mechanisms of the body. Facts which seem to support this view are that the same kind of tumor or growth in two different individuals may react very differently under exactly similar amounts of radiation. This is as well marked in benign growths, such as uterine fibroids, as in cancer. Viewed from this standpoint it would seem that a favorable effect from radium is obtainable only in such bodies as have definite immunizing substances in their fluids and tissues. That, however, certain tumors are much more easily injured, or that much more natural resistance against them exists, is shown by the fact that certain growths disappear with slight radiation and in a large percentage of cases, while others show just the opposite tendency. Another observation indicating the importance of the body resistance is afforded by the fact that active tubercular glands will disappear in a few weeks under a radiation which has little or no effect on tubercle bacilli growing in culture outside the body. It should be borne in mind clearly, however, that certain neoplastic tissues are but little influenced by radiation, and also that there is an immense difference in the resistance of different normal tissues. Lymphatic organs are particularly sensitive to radiation and are very easily destroyed. The endothelium of blood and lymph vessels is likewise quite sensitive. After radiation it tends to swell up and occlude the lumen of the vessels. The avascularity of radiated tissues after a few months is pronounced. Cartilage, bone and ordinary connectve tissue are generally very resistant. The hair follicles, the glands of the skin, the reproductive parts of the ovary and testicle are very easily injured. We might go on multiplying examples indefinitely.

Not only does the degree of change vary, but also the latent period of change. This is dependent both on the character of the radiation and the character of the tissue treated. For example, if sufficient radiation with soft beta rays is given to produce erythema of the skin, this condition will appear in a week on the average. If such an erythema is produced by hard gamma rays it may not appear until the fourth week after the radiation, or even later. Taking another example to show the difference in tissues, a radiation with gamma rays may cause the disappearance within 48 hours of a large lymphosarcoma. Equal radiation given to a carcinoma of the cervix may produce no visible change whatever in five or six days, but nevertheless leads to the entire disappearance within five or six weeks.

It is evident that the histological changes will vary greatly with the tissues treated. Taking the cervix carcinoma as an example one finds in three or four days a tendency for the nuclei of the cells to swell and the protoplasm to become vacuolated; at the end of two weeks many of the cells are disintegrating; at the end of four weeks all carcinoma cells may have disappeared and in their place a new connective tissue formed; at the end of several months there is a great deal of connective tissue and a marked diminution in the vascularity of the part. Nerve and brain tissue are fortunately very resistant. Any injury to these tissues from radiation would seem to be due to changes in the blood-vessels supplying them.

So much for a hasty review of general principles. Now for a brief summary of clinical results and suggestions as to value.

Radium in Gynecology.

Perhaps the most striking effect of radiation in this specialty is in

its certain control of excessive uterine hemorrhage due to metropathies, or disturbed ovarian function. Every gynecologist has to deal with those women who either bleed continuously or excessively in abnormally prolonged menstrual periods. Such cases are commonest in very young girls or in women past 40, but occur at any age. In some of these cases there is formed a polypoid condition of the endometrium, in others simply a slightly enlarged hard uterus. Even the milder cases suffer from the results of anæmia, and in the severer forms the patient may actually die from hemorrhage, unless relieved by operation or by radium. While palliative operations, particularly curettage, give temporary relief, permanent relief is, as a rule, only obtained by hysterectomy. The use of radium offers a far simpler and safer procedure. Usually a single application of 300 mg. for three hours intra-uterine causes a permanent amenorrhea. A second application can be given in six weeks if the first fails in the desired result. These patients pick up rapidly generally, suffer no inconvenience and are usually,in more than 50 per cent. of the cases, free from hot flushings or other menopausal symptoms. In very young women the treatment is greatly shortened, with the result that menstruation is rendered normal in type so far as duration and loss of blood are concerned. It is only the very occasional case that has to be treated to complete amenorrhea to secure a perfect restoration to health.

Hemorrhage associated with fibroid tumors of the uterus is likewise and in the same way readily controllable, and in addition the tumor itself will either completely disappear or be reduced to an insignificant size. About five per cent. of the cases treated do not decrease in size. Some of these are calcified fibroids and in others the patient lacks the necessary solvents in her blood. Neither the size nor the position of the tumor are of moment. The rate of disappearance varies greatly. After a single radiation one tumor may disappear in two months; another only after six or eight months. In some cases large uterine fibroids disappear without any effect on the periodic, normal recurrence of menstruation. Tumors in women past the menopause also readily go down. This treatment is without danger, it is usually accomplished in a single radiation, and is in our opinion the procedure of choice. Operation should be limited to fibroids complicated by other pelvic conditions and to those which do not yield to the radium treatment.

Foreign observers report successful results in cancer of the body of the uterus. We have seen large, recurrent, abdominal, metastases of this type of cancer go down rapidly, but no cases were cured. The results of operation are so good, and the difficulties of determining the extent of the cancer so great, that as yet we have not tried radium in a single operable case, nor would we advise its use in any person except where some general complication precluded operative interference.

In cancer of the cervix uteri and of the vagina most remarkable results are possible. The hard, scirrhous cancer of the cervix is the most resistant type, and the cellular, slow growing medullary carcinoma, especially that which tends to spread over the vaginal wall, is the most favorable. It is easily possible to radiate away metastases in the vagina, bladder and rectum, without interference with the integrity of these viscera. A huge, inoperable carcinoma fixed to either pelvic wall can within a few weeks appear clinically healed, and some of these patients stay healed for at least several years. Where healing does not occur there is almost invariably improvement in the general condition, bleeding

and discharge cease, and pain is diminished or disappears. We have seen not only the parametria clear up, but also regional lymph glands. There can be no question that radium is a great boon to patients suffering with inoperable and recurrent cancer of the cervix uteri. It is equally certain that its use in operable cases, along with operation, will greatly increase the number of permanent cures. It is still uncertain whether operable cases should be treated with radium alone. It seems likely that there are curable cases from operative treatment which would resist radiation, owing to a lack of protective resistance in the patient's own body. In the future, much greater care must be exercised in reporting cancer results. Great detail must be given as to the type of growth, its method of extension, its actual extent, etc. It may develop under such criteria that those cases which resist radiation also become general from their very incipiency. For the present it seems sound advice to follow out both treatments, and to limit the radiation alone to those patients who have some general contra-indication to operation.

The fourth class of patients who are unusually benefited by the treatment are the pruritus and kraurosis vulvæ sufferers. It is truly astonishing in these patients to see the itching disappear and the skin return to normal. Usually two or three mild applications suffice to bring about this result.

Ovarian tumors, tumors of the vulva and the other gynecological conditions have given much less satisfactory results, and our results are not at present in a position to be reported upon.

Radium in Genito-Urinary Disease.

The papilloma and papillary carcinoma of the bladder are favorable tumors, although the amount of radiation has to be greater than in the cervical carcinoma. The squamous-celled cancer of the bladder is very resistant; tubercular ulcers and other chronic ulcers are quite favorably influenced. We have under observation several patients with simple hypertrophy of the prostate gland, who seem to be greatly improved by the radium treatment. We have also one case of prostatic carcinoma apparently cured. It would seem that the conditions of the prostate offer an extensive and promising field for the trial of radium radiation. Comparatively little is at hand in the foreign literature in regard to these patients.

Radium in Rectal Disease.

Adenocarcinoma, especially that just above the sphincter region, is definitely curable in some cases and beneficially influenced in almost all. The squamous-celled cancer of the anus is much less readily influenced. Multiple polyposis does remarkably well. In both the rectal and vesical cases radiation treatment is indicated in the early stages when the operation means serious mutilation. If it fails, operation can be resorted to. In operative cases, both the permanency and the percentage of cure will be increased by a combined treatment. Some inoperable cases are undoubtedly curable.

Radium in Abdominal Tumors.

The most striking results are obtainable in the retroperitoneal sarcomata. We have some immense growths of this type which have completely disappeared, and a few which have been free from recurrence for months. The colloid carcinoma of the intestine does not do so well as that of the thyroid gland, but nevertheless is a condition in which radium treatment offers great hope. Several cases have been

clinically well over long periods. We have had no definite cures in stomach or liver carcinoma, having seen only very advanced cases. Werner of Heidelberg, *Strahlentherapie,* vol. 5, part 1, p. 10, reports several cures. This important field has just been touched. It would seem that an intelligent combination of surgical and radiation treatments might lead to a very great improvement in the present methods of treatment. It is of interest that ascites due to abdominal cancer is occasionally completely done away with by radiation. Among unusual conditions we have observed in a girl the complete disappearance of a sarcoma of the left kidney. In a man with a hæmoglobin of 120, marked cyanosis, difficulty in breathing and an immense spleen, a thorough radiation of the spleen has resulted in a return to normal of the blood and spleen, and apparent perfect health, which has persisted for several months.

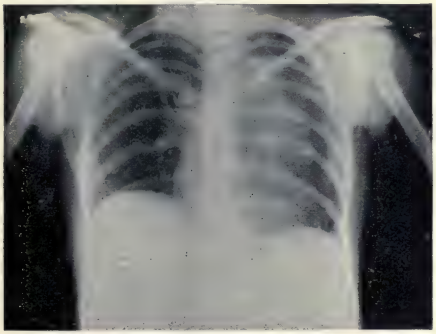

Fig. 1.—Sarcoma of the mediastinum before treatment.

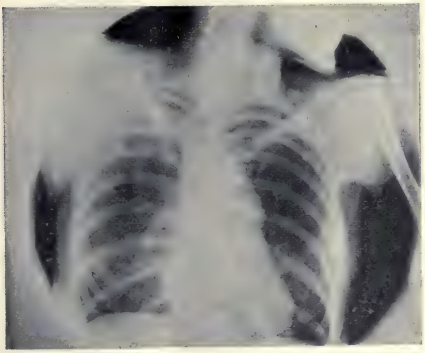

Fig. 2.—Sarcoma of the mediastinum after treatment.

RADIUM IN THORACIC TUMORS.

Werner, *loc. cit.,* as well as N. S. Finzi, *Radium Therapeutics,* 1913, report healed carcinomata of the œsophagus. In four or five cases we have not succeeded in obtaining a single cure so far, although there has been some benefit in most of them. Several large, mediastinal

tumors have disappeared completely. One of these is illustrated in the case of Mrs. R. L., age 30, who had a large mass filling the mediastinum, extending into the neck and into the left pleural cavity. Her general condition was good except for a little dyspnœa. A small piece of tissue removed from the neck showed that the tumor was a small round cell sarcoma. Under treatments given in July and August, 1913, the growth began rapidly to disappear and had entirely gone in two months. This condition has now lasted more than a year and is well shown in the skiagrams of the chest, Figs. 1 and 2, the first of which was taken before radiation, and the second six months later. A third plate recently obtained shows the same condition as in Fig. 2.

Radium in Tumors of the Breast.

The malignant tumors of the breast are in general sensitive to radiation. This is especially true of the softer and more voluminous types. Not only do the primary growths yield, but also the axillary and supra-clavicular gland metastases. In patients with mediastinal and

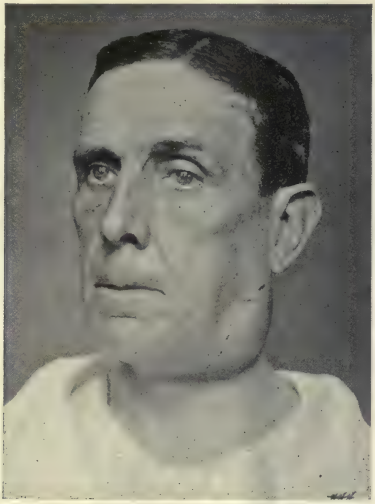

Fig. 3.—Sarcoma of the naso-pharynx, mouth and glands of neck before treatment.

lung involvement, radiation is contraindicated. We have a number of patients apparently well of local recurrences after operation, where thorough radiation has been given. It is our impression that operable breast cases should have the combined treatment; that inoperable and recurrent cases should be given radium radiation as long as the trouble remains regional. It will take a long period of observation and study to definitely give radium its value in the treatment of malignant tumors of the breast, but there is certainly good evidence that it is a valuable adjuvant to our existing measures of treatment.

Conditions of the Thyroid Gland.

Large colloid goiters frequently, rapidly and almost completely regress. Colloid carcinoma of the thyroid gland is a very favorable growth. We have one very extensive recurrent case apparently cured.

Exophthalmic goiter, especially where there is thymus involvement, we have improved almost invariably, but as yet have not obtained a definite cure such as is obtained by thyroidectomy in many cases. Dr. Robert Abbe has reported favorable cases belonging to this group. We feel that with careful investigation and working out of proper techniques there is an extensive field for trial of radium in treating disorders of the thyroid gland. It should always be tried in thyroid malignancy, either alone or as an adjunct to operation.

Conditions of the Larynx.

There is reasonable ground for believing that tubercular ulceration of the larynx can be greatly benefited by radiation. The percentage of carcinomata, especially those belonging to the papillary and basal-celled types, that can be cured is fairly large. We have three cases well for more than a year, and several others well for shorter periods. These patients have been treated almost exclusively by radiation from the

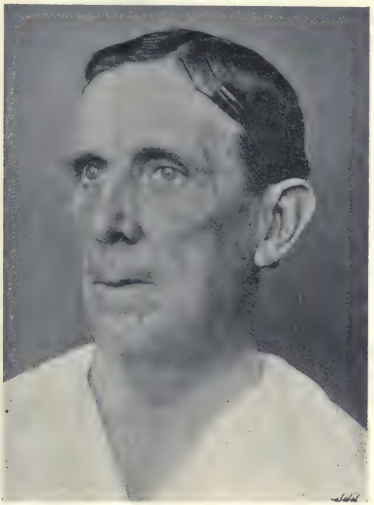

Fig. b.—Sarcoma of the naso-pharynx, mouth and glands of neck after treatment.

outside. Considering the usual hopelessness of these patients radium seems to be of great value here, competing most favorably with the mutilating laryngectomy.

Radium in Tonsillar Disease.

The basal-celled epithelioma and the sarcomata are unusually favorable, even when they have extended to the glands of the neck. As these cases are incurable surgically, we feel that the small group of apparently cured cases is a real triumph. The spinous-celled carcinoma of the tonsil is unfavorable, but can be helped and cured in some cases. In this tumor the burying technique is extremely valuable.

Radium in Mucous Membrane of the Mouth.

With the exception of the lip epitheliomata, the mucous membrane cancers of the mouth are harder to deal with than similar growths on the skin. The tongue cases are particularly difficult and disappointing.

Wherever possible in these growths, which are mostly spinous-celled epitheliomata, the radium should be used in conjunction with surgical treatment.

Conditions of the Naso-pharynx.

The tumors of the naso-pharynx are many of them sarcomata and are practically all incurable, but yield to radium a most gratifying field. It is truly astonishing to see how some of these immense growths clear up and seem to remain well. Figs. 3 and 4 are photographs of a patient admitted in the hospital on May 23, 1914, with an immense tumor filling the naso-pharynx and extending into the glands of the neck on both sides. When first seen he could not speak, and could hardly swallow because the tumor pressed the palate down against the teeth. Tissue removed showed round-celled sarcoma. The patient was immediately radiated and by June 2 the tumor had entirely disappeared. This man

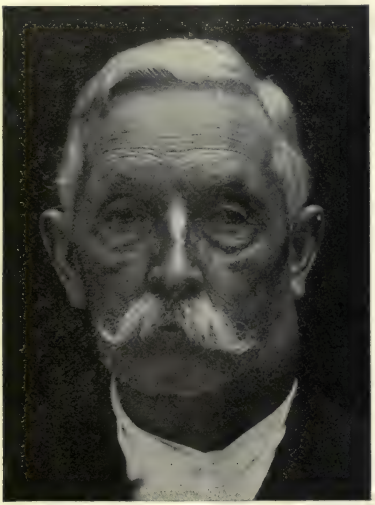

Fig. 5.—Sarcoma of neck before treatment.

has remained well ever since. This patient is typical of a considerable number whom we have had opportunity to consider and treat.

Conditions of the Neck.

The primary sarcomata, particularly the small round-celled and angio-types, do extraordinarily well. It is very common to see the complete disappearance of a large tumor after a single thorough radiation, such as is shown in Figs. 5 and 6. The first of these photographs represents conditions prior to operation, and the second those found after the radium treatment. It is also of interest that this patient, who became clinically well in two weeks, has remained so for nearly 18 months. The metastatic cancers do not do very well in most cases. Hodgkin's disease and tubercular glands are both most favorably influenced. Our experience to date indicates that in the susceptible sarcomata radiation alone is preferable to operation or to operation

and radiation. In the unsusceptible sarcomata and carcinomata operative and radium treatment should be combined wherever possible.

Conditions of the Skin.

Skin sarcomata, including the melanotic form, are quite susceptible to radiation. The basal-celled epitheliomata of the rodent ulcer type respond well in a large percentage of cases, even when very extensive. The spinous-celled epitheliomata are much more resistant. In this class it would seem wise, as in any epithelioma which is resistant, to combine the radiation with surgical procedure. The inoperable cases, however, are an exeception, except where the actual cautery and radium can co-operate. It is most important in these patients not to be satisfied with an apparent cure, but to keep under observation and re-radiate for at least two years. Among non-malignant skin diseases there is the greatest variety which can be helped; birthmarks of the port wine type,

Fig. 6.—Sarcoma of neck after treatment.

of the angiomatous type, of the pigmented and hairy mole type, acne rosaceæ, lupus erythematosus, rhynophyma, lupus vulgaris, macrocheilia, macroglossia, offer peculiarly favorable conditions.

General Conclusions.

The statements included in this paper are founded on personal observations. I have made no attempt to take results from other observers. My aim has been to enlist your interest and to point out that radium has a wide field of usefulness, the boundaries of which have not been fixed and can only be determined by long, painstaking statistical studies. We do not believe that radium has any field absolutely to itself. It is merely an extraordinarily, widely applicable, therapeutic agent, which must be used intelligently in connection with all other known methods of treatment. In connection with the treatment of benign growths it would seem that owing to its mildness and

lack of danger it might be tried as a preliminary, and surgery reserved for the cases it fails in. With malignant growths, where surgery offers hope, the two methods had best be combined. With malignant growths which are inoperable, hope is held out by the radium treatment, and especially is this true in many sarcoma cases. It is our opinion that in certain types of sarcomata which have not proved curable by surgery, even in the earlier stages, the radium treatment should be used alone even when the growth is very small. The radium treatment is also of great advantage in operable cases of malignant growth where the operation means great disfigurement and mutilation. Examples are furnished by the epitheliomata about the eyes, on the nose, the rectal and vesical sphincters, etc. While it is also probable that even in the earlier stages, where the body resistance of the patient is at its best, that no one type of tumor is curable in all cases and some in only a small percentage of cases, it does not mean that this condition of affairs need permanently exist. Better methods of radiation ought to greatly improve results, but what seems even more important is work to determine the cause of the difference in resistance in individuals and if possible to develop methods of increasing this resistance. It would seem that all the vaccines, serums and specific drugs which have been brought out in the last decade as agents for treating cancer, and many of which have apparently given results in a few cases, will have to be tried over again in combination with radiation. It is also most important that careful, comparative investigations with the X-ray be carried out, and the degree of overlapping, with the possibilities of uniting the two methods be determined. The possibilities of using X-ray as a therapeutic agent have been tremendously increased through the technical developments of the last few years. It is possible now to give a uniform dose with the X-ray and it is also true that the character of the X-ray, so far as its penetration is concerned, is steadily approaching that of the gamma ray of radium. The surgical uses of radium embrace a field much wider than that of the treatment of neoplasmata. The effects on secretory glands, on neuralgias, on local tubercular and other conditions, must be borne in mind. It is also evident that the medical uses of this drug may be considerable.

REVIEWS AND ABSTRACTS

Sir Ernest Rutherford, F.R.S. Radiations from Exploding Atoms.* Nature, July 1, 1915. A discourse delivered at the Royal Institution, London, on Friday, June 4. "It is now well established that the radio-active substances are undergoing spontaneous transformation, and that their characteristic radiations, the alpha, beta, and gamma rays accompany the actual disintegration of the atoms. The transformation of each atom results from an atomic explosion of an exceed-

*Professor Rutherford in this lecture gives a brief resume of the present state of our knowledge respecting the rays of radio-active substances, the structure of the atom, the inter-convertibility of beta and gamma rays, and the relation of the gamma and X-rays. Such parts of the lecture as seemed of interest to the general reader, have been reproduced in full. The discussions of the alpha rays, and of the quantitative relation between the groups of rays in a beta-ray spectrum and the emission of characteristic gamma rays, (including Planck's relation) have been omitted. The relation between the gamma rays and X-rays has been a much discussed point by those interested in radio-therapy, and it is most valuable to have a clear statement of the present knowledge of this subject from an authority. Ed.

RADIUM

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ingly violent character, and in general results in a liberation of energy many million times greater than from an equal mass of matter in the most vigorous chemical reaction."

"In the majority of cases the atomic explosion is accompanied by the expulsion of an actual atom of matter—an alpha particle—with a very high speed. It is known that the alpha particle is an atom of helium which carries two unit positive charges, and which leaves the atom with a velocity of about 10,000 miles per second. In some transformations no alpha particle is ejected, but its place is taken by a swift beta particle or electron. These beta rays carry with them a large amount of energy, for in some cases they are expelled very close to the velocity of light, which is the limiting velocity possible for such particles. The expulsion of high speed beta particles is usually accompanied by the appearance of gamma rays, which correspond to X-rays, only of greater penetrating power than has so far been obtained from an X-ray tube, even when a high voltage is employed. The emission of energy in the form of gamma rays is not negligible, for in some cases it is even greater than the energy emitted in the form of high-speed beta particles, and may amount per atom to as much as 20 per cent. of the energy released in the form of a swift alpha particle."

"By the application of a high voltage to a vacuum tube, it is quite possible to produce types of radiation analogous to those spontaneously arising from radium. For example, if helium were one of the residual gases in the tube, some of its atoms would become charged and would be set into swift motion in the strong electric field. In order, however, to acquire a velocity of expulsion of an alpha particle, say, from radium C, even in the most favorable case, nearly four million volts would have to be applied to the tube."

"In a similar way, in order to set an electron in motion with a velocity of 98 per cent., the velocity of light, at least two million volts would be necessary. As we have seen, it has not, so far, been found possible to produce X-rays from a vacuum tube as penetrating as the gamma rays. The study of radiations from radio-active substances is thus of special interest, not only for the information obtained on the structure of the atoms themselves, but also in providing for investigation special types of radiation of greater individual intensity, than can be obtained by ordinary experimental methods. The enormous energy of motion of swift alpha and beta particles must exist in the atom before its disintegration, either in a potential or a kinetic form, and may arise either from the passage of the charged particles, through the intense electric fields within the atom, or from the very swift motion of these particles, within the atom before their release. In any case, there can be no doubt that electric fields, and possibly magnetic fields, of enormous intensity exist within the very small volume, occupied by the essential structure of the atom—fields many million times greater in intensity than we can hope to produce in laboratory experiments."

"In order to explain experimental results, I have suggested that the main mass of the atom is concentrated within a minute volume or nucleus, which has a positive charge, and is of dimensions exceedingly minute compared with the diameter of the atom. This charged nucleus is surrounded by a distribution of electrons, which may extend to distances comparable with the diameter of the atom, as ordinarily understood. The general evidence indicates that the alpha and primary beta particles are expelled from the nucleus, and not from the outer structure

of the atom. If this be the case, the alpha particle, which carries a positive charge, would have its velocity increased in passing through the strong repulsive field surrounding the nucleus; on the other hand, the beta particle, which carries a negative charge, must be retarded in its escape from the nucleus, and must possess great initial energy of motion to escape at all. There appears to be no doubt that the penetrating gamma rays have their origin in some sort of disturbance in the rings of electrons nearest to the nucleus, but do not represent, as some have supposed, the vibrations of the nucleus itself."

Beta Rays. "During the last few years notable advances have been made in our knowledge of the mode of emission of beta particles from radio-active atoms. The work of Baeyer, Hahn, and Meitner, and of Danysz, has shown that the beta rays from a radio-active substance, like radium B or radium C, contain a number of definite groups of rays, which are expelled with definite velocities. This is best shown photographically by examining the deflection of a pencil of beta rays in a magnetic field. In a uniform field, each of the groups of rays describes a circular path, the radius of which is inversely proportional to the momentum of the beta particle. By the application of special methods it has been found possible to obtain a veritable spectrum of the beta rays. The spectrum of the beta rays from radium B and radium C has been very carefully examined by the writer and Mr. Robinson, and found to give a large number of well-marked bands, each of which represents a group of beta rays, all of which are expelled with identical speed. It was at first thought that most of the energy of the beta rays was comprised in these groups, as some of the bands on the photographic plate were very marked. Chadwick, however, has recently shown that the fraction of the rays which give a line spectrum is only a few per cent. of the total radiation. The general evidence shows that the beta radiation from these substances gives a continuous spectrum, due to beta rays of all possible velocities, on which is superimposed a line spectrum due to a small number of beta particles of definite velocity comprising each group."

"Lines in the beta ray spectrum have been observed for particles, which have a velocity not far from that of light, but the photographic effect of the particles becomes relatively feeble for such high speeds."

"It is known, from direct measurement, that each atom of radium B or radium C, in its disintegration, emits on an average one beta particle. In the beta ray spectrum of radium C, at least fifty definite bands are observed, differing widely in intensity. It is thus clear that a single atom in disintegrating cannot provide one beta particle for each of these numerous groups. It is thus necessary to conclude that each atom does not emit an identical radiation. The results are best explained by supposing that the beta ray spectrum is the statistical effect, due to a large number of atoms, each of which may only give one or two of the groups in its disintegration. In this respect a beta ray transformation is distinguished from an alpha ray transformation, for in the latter case each atom emits one alpha particle of characteristic speed."

Gamma Rays. "The earlier experiments on the gamma rays were mainly confined to a determination of the absorption of the more penetrating radiations by different kinds of matter. It was early observed, however, that some of the radiations appeared to be complex. This was shown by anomalies in the initial part of the absorption curve. In the meantime, a notable advance in our knowledge of X-rays had been

made by the work of Barkla. He found, that under certain conditions, each element, when bombarded by X-rays of suitable penetrating power, gave rise to a strong radiation, which was characteristic for that element, e. g., the lighter elements from aluminium to silver emitted characteristic radiations called the "K" series, which increased rapidly in penetrating power with the atomic weight of the radiator. It was found that the heavier elements emitted in addition another characteristic radiation of softer type, which was called the "L" series. These results showed clearly that there must be definite structures within the atom, which give rise to a definite radiation under suitable conditions of excitation. From these results it seemed probable that the gamma rays from radio-active matter must consist of the characteristic radiations of these heavy elements, analogus in type to the corresponding radiations observed in ordinary elements, when excited by X-rays or kathode rays. These conclusions were confirmed by a series of investigations made by Rutherford and Richardson. The gamma rays were analysed by means of their absorption by aluminium and by lead, the disturbing effects of the primary beta rays being eliminated by means of a strong magnetic field. It was found, for example, that the gamma rays from radium B, when examined by their absorption in aluminium, consisted of at least two types, one easily absorbed, and the other eighty times more penetrating. By further observations of the absorption of the gamma rays by lead, Richardson found that the rays from radium B could be divided into at least four definite types, each of which was absorbed exponentially by lead. Similar results were obtained for all the radio-active elements, which emitted gamma rays. In some cases the soft gamma rays, e. g., those from radium B, corresponded to the characteristic radiation of the "L" series, and others to the "K" series. The general results, however, indicated that several additional series of characteristic radiations are present in some cases. It was clear from these experiments that the gamma rays corresponded to the natural modes of vibration of the inner structure of the radio-active atoms. In the meantime, the experiments of W. H. Bragg and W. L. Bragg, and of Moseley and Darwin, had shown that the characteristic X-radiations of the elements gave definite and well-marked line spectra. These spectra were simply determined by reflecting the rays from crystals. If this were the case, it seemed probable that the gamma rays from the radio-active atoms would also give line spectra, and thus allow the natural frequencies of vibration of these atoms to be determined. During the past year, a number of experiments have been made to test this point by Rutherford and Andrade, using radium B and radium C as the source of gamma radiation. As was anticipated, it was found that the gamma rays from radium B and radium C gave well-marked line spectra. The general method employed was to use an alpha ray tube containing a large quantity of emanation as a source of radiation. The gamma rays were reflected from a crystal of rock salt, and the position of the spectrum lines determined photographically. Usually twenty-four hours were necessary to obtain a marked photographic effect. Special difficulties arose in these experiments, which are absent in an investigation of a similar kind with X-rays. In addition to gamma rays, the radio-active matter emits very penetrating beta rays, which have a strong photographic action; while the gamma rays in their passage through matter themselves give rise to high-speed beta rays. The disturbing effect of these radiations has to be eliminated by placing the whole apparatus between the

poles of a powerful electromagnet. In this way it was found that the spectrum of radium B consisted of a large number of lines, of which the most intense were deflected at angles of 1° 46′, 10°, and 12°. The more penetrating radiation from radium C gave a strong line of 1° and a fainter line at 43′. The strong lines at 10° and 12°, are due to easily absorbed gamma rays, and undoubtedly correspond to the "L" radiation of radium B. The line at 1° corresponds to a very penetrating radiation, which has a wave length less than 1/10th of an Angstrom unit. The penetrating gamma rays from radium C have by far the shortest wave length so far observed. It does not seem probable that such short waves can be produced artificially in an X-ray tube, unless possibly an exceedingly high voltage be applied."

"There is one interesting result of these investigations that should be mentioned. The two strong lines of the radium B spectrum deflected at 10° and 12°, were found to correspond exactly in position to the X-ray spectrum of lead. These experiments thus confirmed the view based on chemical evidence that radium B and lead were isotopic, i. e., they were elements of practically identical chemical and physical properties, although their atomic weight differed by seven units."

"Connection Between Beta and Gamma Rays. The main facts that have been established in regard to the relations between kathode rays and X-rays may be summarized as follows:

"(1) A small part of the energy of kathode rays falling on a radiator is converted into X-rays, the average frequency of the latter increasing with the velocity of the kathode particle."

"(2) X-rays in passing through matter give rise to a beta radiation. The initial energy of the escape of the electrons increases with the frequency, and is probably proportional to it."

"(3) Electrons or X-rays of appropriate energy are equally able to excite the characteristic radiations in an atom."

"The results which have been shown to hold for the X-rays, hold equally for the beta and gamma rays, which have much greater individual energies, e. g., Gray and Richardson have shown that the beta rays from radio-active matter are able to excite the characteristic radiations of the elements in a number of substances, while gamma rays, in passing through matter, give rise to high-speed electrons. It was long ago suggested by Bragg that beta rays and X-rays are mutually convertible forms of energy, e. g., a beta particle falling on matter may be converted into an X-ray of the same energy, and the latter, in passing through matter, may in turn be converted into an election of identical energy. This assumes that the energy of an X-ray and an electron are mutually convertible, and the energy may appear under suitable conditions in either of the two forms. While the general evidence indicates that this point of view may hold closely for the conversion of the energy of a single X-ray, into that of a swift electron, it is very doubtful whether it holds for the converse case of the excitation of an X-ray into an electron. We shall see later from experimental evidence that in general the energy of the electron required to excite an X-ray of definite frequency is always greater than the corresponding energy carried off in the form of an X-ray."

"It was early observed that there appeared to be a close connection between the emission of beta and gamma rays from radio-active matter. In all cases, two types of radiation appeared together. A closer examination, however, showed that there were very marked differences between

the relative energies of the beta and gamma rays from different radio-active elements. For example, radium C emits intense beta rays and also intense gamma rays; on the other hand, radium E emits intense beta rays over a wide range of velocity, but exceedingly weak gamma rays."

"An explanation of the marked differences in the character of the beta and gamma radiation from different radio-active atoms can, I think, be given on the following lines. Some of the gamma rays are broken up in their escape from the atoms, and the energy of each converted gamma ray is transferred to an electron, which escapes with a definite velocity dependent on the frequency of the gamma radiation. Taking into account a large collection of disintegrating atoms, each of the possible modes of characteristic vibration of the atom gives rise to an electron of definite speed. In this general way we may account for the line spectrum of the beta rays, which is so commonly observed. On this view, we should expect to obtain a well marked line spectrum of beta rays, when a substance emits strong gamma rays—a result in accord with observation."

"In order to account for the marked differences in the types and intensity of gamma rays from different radio-active substances, it seems necessary to suppose in addition, that the primary beta particle always escapes from the nucleus in a fixed direction with regard to the structure of the atoms under consideration. For example, we have alrady pointed out that radium E, although it emits intense beta rays, which give a continuous spectrum over a wide range of velocity, emits very weak gamma rays. Since there can be no doubt that the beta rays have sufficient speed to excite the characteristic modes of vibration, which must be present in the atom, we are driven to the conclusion that the beta particle escapes in such a direction, that it does not pass through these vibrating centres. On this view, the type of characteristic gamma rays, which are excited, and consequently also the corresponding speed of the beta rays, which arise from the converted gamma rays, will depend entirely on the direction of escape of the primary beta particle. The definite direction of escape of the primary beta particle, which varies from atoms of different substances, also suffices to explain a number of other differences observed in the mode of release of energy from various radio-active atoms. It is supported by many other observations, which indicate that the atoms of a particular radio-active substance break up in an identical fashion."

Limit to the Frequency* of Vibration of the Atom. "There is one question of fundamental importance, which arises in considering the modes of vibration of the atom, viz., whether there is a definite limit

*Hertzian electric waves, radiant heat waves, visible light, ultra-violet light, Roentgen rays and gamma rays are all propagated in the hypothetical medium called the luminiferous aether by an oscillating or wave-like disturbance, the direction of propagation being at right angles to the direction of vibration. The velocity with which these various forms of energy is transmitted is constant, 300,000,000 meters (186,000 miles) per second. Each of these different types of rays is characterized by its wave length, the wave length of the Hertzian rays being greatest and that of the hard gamma ray from radium C being the smallest known. The frequency of a given wave or ray is the number of vibrations made in a second or the number of times that the wave length will go into 300,000,000 meters. The Angstrom unit (1/10,000,000 of a mm.) is commonly used in expressing the wave lengths of light. The wave lengths for visible light range from about 4,000 to 7,000 Angstrom units. The hardest X-rays have a wave length of about 1 Angstrom unit, and the hard gamma rays from radium C have a wave length of about 0.1 Angstrom unit, therefore the frequency of such gamma rays would be 300,000,000,000/0.000,000,01 or 30,000,000,000,000,000,000. This large number probably represents the rate of vibration of the part of the radium C atom which sets up the hard gamma ray having this vibration frequency.—Ed.

to the frequency of the radiation, which can be excited in a given atom. Theory does not provide us with an answer to this problem, since little is known about the conditions of excitation, nor even of the nature of such high-frequency vibrations. A study of the frequency of the gamma rays from radio-active substances is of great importance, as it throws much light on this problem."

"As we have seen, the energy of the beta particle, escaping from the nucleus of radium C, is equivalent to that acquired by an electron, moving in an exhausted space, under a potential difference of several million volts. This high-speed electron passes through the electronic distribution in its escape from the atom. Notwithstanding such ideal conditions for the excitation of high-frequency radiations of the atom, the highest frequency in the radiation emitted by radium C, is only about twice that obtainable from an ordinary hard X-ray tube, excited by 100,000 volts. It thus appears probable that there is a definite limit to the frequency of the radiation obtainable from a given atom, however high the speed of the disturbing electron. This limiting frequency is determined, not by the speed of the electron, but by the actual structure of the atom. Since the gamma radiation from radium C gives a line spectrum, it would appear that the highest frequency obtainable, is due to a definite system of electrons, which is set into characteristic vibration by the escape of a beta particle. In order to throw further light on this point, Prof. Barnes, Mr. H. Richardson and myself have recently made experiments to determine the maximum frequency obtainable from an X-ray tube for different constant voltages. The Coolidge tube, which has recently been put on the market, is ideal for this purpose, as it provides powerful radiation at any desired voltage. The anti-kathode is of tungsten of atomic weight 184, so that we are dealing in this case with the possible modes of vibration of a heavy atom. The maximum frequency of the radiation was deduced by measuring the absorption by aluminium of the most penetrating rays emitted at different voltages. The absorption of gamma rays of different frequencies by aluminium has been examined over a very wide range, and can be expressed by simple formula. It was found that for 20,000 volts the frequency of the radiation was slightly lower than that to be expected if Planck's relation held. With increasing voltage there is a rapid departure from Planck's relation. The frequency reaches a maximum at about 145,000 volts, and no increase was observable up to the maximum voltage employed, viz., 175,000 volts. The experiments thus show that the frequency of radiation reaches a definite maximum, which is no doubt dependent on the atomic weight of the particular radiator employed. It is of interest to note that the maximum penetrating power of the X-rays from the Coolidge tube in aluminium is about the same as the gamma rays from radium B, but is about 3/10 of the the gamma rays from radium C. There is evidence which suggests that the very penetrating gamma rays from radium C correspond to the octave of the "K" characteristic radiation of that element. If this be the case, it may prove possible that a still more penetrating radiation might be obtained from tungsten, but in order to excite it a voltage of the order of a million volts would probably be required."

"There can be little doubt that the penetrating gamma rays from active matter have their origin in the vibration of electronic systems in the structure of the atom outside the nucleus. The nucleus itself, however, must be violently disturbed by the expulsion of an alpha or beta

particle. If this leads to the emission of a gamma radiation, it must be of exceedingly high frequency, as the forces holding together the component parts of the nucleus must be exceedingly intense. We should anticipate that this radiation would be extraordinarily penetrating, and difficult to detect by electrical methods. So far no experimental evidence has been obtained of the existence of such very high frequency radiations, but it may be necessary to devise special methods before we can hope to do so."

* * * * *

Brooke M. Anspach, M.D. (Philadelphia, Pa.). The Treatment of Advanced Carcinoma of the Cervix with Radium. The American Journal of Obstetrics, July, 1915, pp. 97-101. Read at the meeting of the Philadelphia Obstetrical Society, February 4, 1915. "My experience to date comprises five cases. As a result of the treatment, in two the subjective and objective symptoms have almost entirely disappeared; two are very much relieved; one has been failing in health. All the cases are still under observation. All but one are recent."

"The first, and much the oldest case, had so many interesting and striking features, that I venture to present it in detail."

"The patient, a woman of sixty-one, consulted me in August, 1912, and at that time presented the usual symptoms of an advanced carcinoma of the cervix, extended to the posterior vaginal fornix, and hopeless from the standpoint of a radical cure. I advised the customary procedure of curetment and cauterization, which was carried out on the following day. The patient after recovering from a sharp attack of ether pneumonia, went to the home of her sister in a neighboring town, and there was treated with applications of acetone. Her condition steadily grew worse. The discharge became profuse and extremely offensive; she lost strength and weight, and became bed-ridden."

"In December of that year (1912), Dr. John G. Clark and his staff visited Dr. Howard Kelly in Baltimore, who told us of his investigations of radium, and spoke hopefully of what it promised in the treatment of inoperable cancer. The point that impressed us as of great practical moment, was that radium had an emanation, which could be compressed into a glass capsule, and had the same therapeutic power, though to a less degree, as radium itself. It was therefore possible to treat patients, even at a distance from the supply."

"The patient I speak of was so far gone that it did not occur to me to use the emanation in her case, but my assistant, Dr. Spaeth, wished to try it, and in this desire he was enthusiastically supported by one of the patient's sisters."

"The first application of the radium emanation was made on the 29th of January, 1913, almost four months after the curetment. The day before, the patient had suffered from an uremic attack, and her condition appeared critical. The family physician advised giving her morphia and letting her die in peace. She was septic, 35 pound below weight, has an extreme degree of anemia, and appeared on the verge of dissolution. One member of the family was extremely adverse to the use of the radium, thinking that some extra torture was to be inflicted upon her mother, and it was only after I had exhibited the tiny luminous capsule to her and explained that all we wished to do was to place it in the carcinomatous area, that she gave her consent."

"A second emanation was used on the 9th of February, and on the 28th of February, about 100 mg. of radium sent up from Baltimore

was placed in the carcinomatous area."

"Almost from the beginning of the treatment, the patient had shown signs of improvement, and within ten days of the first application of the emanation, the odor had diminished very considerably. At the time when the radium was used, an examination showed dense infiltration of both the rectovaginal and the vesicovaginal walls, and considerable infiltration into the bases of the broad ligaments. There was no indication of neighboring or remote glandular involvement or metastases. The radium was left in place two days and three nights. Thereafter the patient experienced severe vesical and rectal tenesmus, which lasted two or three weeks. Her condition aside from this seemed to gradually improve, and has continued so until the present time. I saw the patient last on the 5th of May, 1914, nearly a year ago, and at the time the blood was normal, she had gained 35 pounds, she had no pain, there was no discharge from the carcinomatous area, the rectovesical and the vesicovaginal fistula were nearly closed, and upon digital and visual examination of the area, no evidence of carcinoma could be seen or felt; the tissues were soft and pliable, and to all intents and purposes, the disease had disappeared. The patient still continues to do well, she is gaining in weight and strength, does her own housework, and feels that she has been given a new lease of life."

"The second patient, aged sixty-two, was curetted and cauterized on the 27th of July, 1914. This patient lives in a neighboring city. She came to Philadelphia on two subsequent occasions and had an application of about 25 mg. of radium over night. After the second application she failed rapidly in health, and died in a few months."

"The third patient was a woman forty-four years old; curetment and cauterization was performed August 26, 1914. The case was one of hopeless carcinoma of the cervix. The patient has had three applications of radium. At present she feels and looks perfectly well. It has been hard to persuade her that she still requires treatment. She has no symptoms, no bleeding, no discharge, but there are still some slight evidences of the carcinomatous disease in the neighborhood of the cervix."

"The fourth patient, aged thirty-seven, was operated upon the 9th of October, 1914. She had two treatments with radium; one on November 11, and one on December 29. At the present time there is practically no macroscopic evidence of the trouble. The uterus is freely movable, the carcinomatous area is covered with healthy mucosa, and she has absolutely no symptoms. The improvement in her general health is quite remarkable. At the time of her admission to the hospital, social service workers expecting her to die, had her children admitted to an institution for the care of the destitute. The patient is now having some trouble in having them returned."

"The fifth patient was a woman twenty-eight years old, upon whom I operated October 14, 1914. She came to the hospital for the cure of a complete tear of the perineum. The carcinoma of the cervix, which was advanced, had not been suspected. She attributed all her symptoms to the tear. The woman has had two treatments since. Her general condition has improved very much, she has no symptoms whatever, and the carcinomatous area has shrunken so as to be almost unrecognizable."

"It is scarcely necessary for me to report that there have been

many instances of complete cessation of objective and subjective symptoms of carcinoma following treatment with radium, or mesothorium, of the X-ray, or all combined. The reports of Kroenig and Gauss, Doederlein, Bumm and Voigt, Schauta, Wertheim, Cheron and Duval, Pinch, and others, prove that radium has a distinct and positive influence upon carcinoma cells. It would appear that exposure to the influence of the gamma rays causes the cells to shrink and finally to disappear. Whether they completely disappear depends upon the virulence of the individual growth, the length of exposure to the rays, the amount of radium that is used, and possibly to the individual resistance of the patient."

"It is pretty generally agreed that radium itself is more effectual than mesothorium, and that the filtered rays are therapeutically an improvement on the unfiltered rays. The radium must be used in large dose, and the salt must be placed in immediate contact with the carcinomatous area. It is almost universally agreed that it is a great advantage to combine the use of radium with deep X-ray treatment, and this we are now doing with the three cases which are still under active observation at the University Hospital."

"In summarizing the conclusions, which I have drawn from this study, I may say:"

"First, that treatment by radium must be reserved for those cases of carcinoma of the cervix in which removal by operation is out of the question; it is certainly unwise to depend upon the use of radium alone. Nothing can take the place of operation in an early case. Radium must be used as far as possible in every postoperative case to prevent recurrence. In those unfortunate instances in which the disease has advanced beyond the possibility of radical surgical treatment, radium will cure a percentage not yet determined, and will give the stricken people formerly condemned to die, a new hope."

"Second, the therapeutic effect of radium is probably analogus to the therapeutic effect of the X-ray. Only in radium we have a substance which can be placed directly in the diseased area, overcoming in this way some of the mechanical difficulties encountered with the X-ray in the treatment of cervical carcinoma. Radium will probably prove to be as effectual against certain advanced cancers of the cervix as the X-ray has been curative in certain malignant growths of the skin. The case particularly suitable to such treatment is cancer of the squamous type, which is moderately destructive and invasive, and in which there are no metastases or deep extensions."

"Third, with few exceptions up to the present time, radium has not been used properly. It must be exhibited in massive dose, and the case must be kept under observation until the local subjective and objective symptoms have disappeared. The difficulties in carrying out these recommendations are the enormous cost of radium, the limitations of its supply, and the lack of hospital facilities."

"Fourth, in order to avoid deception in regard to radium treatment of all sorts, the collections of radium should be limited to hospitals and public institutions, and the existence of all radium supplies should be registered in the Department of Public Health, so that fraudulent advertisers and sham preparations of radium can be apprehended."

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In the discussion of papers at the Feb. 4, 1915, meeting of the Obstetrical Society of Philadelphia (Am. Journ. of Obstetrics, p. 157,

July, 1915), comment was made on the use of radium, in the discussion of Dr. Anspach's paper (see preceding article).

"Dr. John G. Clark.—As to the use of radium for the treatment of cancer, I am conservatively optimistic. We cannot ignore for one moment the large accumulation of favorable literature, which has already come before us, detailing the good results obtained by many investigators. Indeed, the results border upon the miraculous."

"Two cases quite recently within my own experience are startling in the quick change for the better. In one, a woman was treated six weeks ago with 85 mg. of radium applied to a cancer in the vaginal fornix, which had formed a crater the size of an English walnut and extended outward to the pelvic wall. An operation was impossible because of the intimate relationship of the ulcer to the ureter. Radium was applied for twenty-four hours. The cancerous area has shrunken to a shallow pit, which does not bleed, and is not more than ½ cm. in diameter and the same in depth."

"Even a more striking instance—a case of chorioepithelioma seen in consultation with Dr. Erck and Dr. Levi. A considerable ulcer existed in the vaginal fornix at the site of a hysterectomy, and in the left vaginal wall there was a fixed mass the size of a lemon, closely attached to the pelvic wall, and in direct relationship with the ureter. In this case, a further operation was considered most inadvisable on account of its radical nature and the extreme hazards attending it, with little or no promise of relief. Radium was at once applied and the mass has shrunken to almost indistinguishable remains. After three days, the bleeding, which had been excessive, ceased, and on physical examination cannot be induced. Even though this case should ultimately succumb from metastasis, which is possible, and indeed probably, the result is nothing less than miraculous. These cases, therefore, indicate the value of radium even in apparently hopeless cases, and it behooves us not to look with such extreme skepticism, as is prevalent among many, upon the results reported by so many competent observers, but at once to apply this treatment in properly selected cases."

"Again, I do not believe that the surgical treatment is abrogated. Indeed, radium should only be utilized in the operative cases as an assurance against recurrence. It must not supercede surgical methods until the data bearing upon its positive value become so convincing that we can no longer feel that we are hazarding the life of the patient by keeping her under this treatment, while surgical methods are still possible. One of the advantages claimed for radium is that a preliminary application will limit the growth, stop hemorrhage and foul discharge and thus decrease the dangers of a radical operation."

"Dr. Henry K. Pancoast.—We have heard to-night several methods of treating malignancy—by the X-ray, operation, dessication and by radium, and each advocate I think has spoken mainly of one of these. It is my belief that the best results are often accomplished by a combination of methods. My short experience with carcinoma of the uterus in connection with radium is limited to the cases seem with Dr. Anspach and to one or two others in the surgical service at the University Hospital, One case that I had directly under my care recently was treated first by cauterization and then by the use of radium in the cervix and X-ray applications through the abdominal wall. When malignant disease is widespread some distance from the cervix the radium rays will be

comparatively inactive at a distance while they may be very active at the point of application. They are many hundred times more active near the tube of radium than a few inches away. Therefore, in a case of this kind I think the X-ray should be used in addition, through the abdomen, through the peritoneum and through other points of entry if required. Widespread disease cannot be properly treated unless there is this combination of methods. I can do no more than say that all Roentgenologists, who have treated cases of fibroids thoroughly agree with all that Dr. Pfahler has said. Our technic is practically the same as his, although we may differ over minor points, and our results have been the same."

"Dr. Richard C. Norris.—The X-ray and radium treatment of uterine cancer is thus far a treatment of hope rather than achievement. Two cases stand out prominently in my experience, which I will mention in detail, because they carry the lesson I have in mind. On the same day two patients came under observation with beginning cancer of the cervix. The clinical pictures were identical. Neither had ever borne children. Operation (hysterectomy) was done on the same day. Microscopic diagnosis was identical. Both patients were then treated by the X-ray by the same man, the late Dr. Leonard, and were afterwards treated with radium. Of these two patients one is well to-day—six years after operation. The other was dead in five months, from recurrence. This means that the pathologist does not yet know the potential pathology in individual cases of cancer. We do not know its cause, nor its clinical and destructive pathological differences. When we shall have this knowledge we may know why in one case the X-ray or radium works almost a miracle and utterly fails in another."

"Too little radium is in the hands of one man to test its full power. At the present time we do not know, unfortunately, that neither surgery, X-ray nor radium will cure all types of cancer, and that in uterine cancer, because it may be of the usually late diagnosis, the results are least encouraging."

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Robert Abbe, M.D. (New York). Roentgen Ray Epithelioma, Curable by Radium. An Apparent Paradox. Journ. Am. Med. Assn. July 17, 1915, pp. 220-21. (Read before the Section on Surgery, General and Abdominal, at the Sixty-Sixth Annual Session of the American Medical Association, San Francisco, June, 1915). "At a section meeting of roentgenologists at the British Medical Association two years ago I was impressed by the large proportion of this noble body of workers, who had suffered from all degrees of Roentgen-ray injuries, from simple hyperkeratosis to amputation of one or more fingers, or one hand, or both."

"I presented to them the possibility of curing the disease in its early stage by radium. Most of them seemed skeptical, but I found one physician from Austria, who had suffered, and who had found in his own experience that radium had kept his hands well, as he had repeatedly applied it in this early type for some years. I showed photographs and spoke of cases which I will here quote:"

"During two years past, I have been more deeply impressed with its importance, as I have treated more cases. Logically, it is clear that if all of the vast number of senile keratoses and early epitheliomas of the face and hands can be cured with certainty by radium, then the early Roentgen-ray growths of the same type ought to yield equally well."

"It is in the advanced stage of epitheliomas, when the downgrowth of cells invades and developes the squamous cell layer—followed by growth of pearls, lymphatic invasion and gland metastases—that no efficient action of radium, so far as we can yet see, is beneficial. Then, anything short of amputation or clean excision is without value. Subsequent to the early stage, however, most sacrifices of fingers and hands have taken place. It is to this point I wish to direct attention, for in the early stage I shall show that cure may be assured."

"My first case so treated was in 1903. Five years after beginning the use of the Roentgen ray, the patient developed a typical epithelioma of the back of the left hand. One application of radium cured it, and there has been no recurrence after twelve years."

"Three years ago a well-known maker of Roentgen-ray tubes came to me with a terrible exhibition of Roentgen-ray cancer of the chin, chest and both hands. One finger had been amputated and much useless surgery done on the other parts. Both hands had on them scores of epitheliomas of varying sizes and heights. A recurrence showed in the stump of the amputated finger, with an enlarged epitrochlea lymph mass of half the size of an egg, and in the axilla and subclavian region of that side, a conglomerate mass resembling a large clenched fist. Hopeless as it all seemed, he wished me to excise the lymph and other related scar growth, and apply radium as well as possible, at least for experiment. This I reluctantly did, much to his delight. During the convalescence he asked me to try what radium would do on the cutaneous epitheliomas, which were, as he said, just the way the original trouble started."

"I used one strong specimen of radium from my collection, and told him I had no doubt they would all be cured by applying it from half an hour to one hour each. In thirty days every one dried up and fell off, leaving a smooth healthy soft scar beneath. Even one with a half-inch base and three-quarters of an inch in height—cornified on top and very vascular at the base—was absolutely cured in the same time. The effect of buried radium in the operated field of the large axillary cancerous masses was, as I expected, of no value. The patient lived some months and succumbed to the cancer saturation, though no recurrence of the epithelial growths took place."

"Many men are living to-day, who have served their profession and the public nobly, who have hanging over them this fate, which has befallen many whom we all know. These may all share the 'exhilarating sentiment of hope' through radium."

"One physician, illustrating a type of severe injury of the hands of one of the pioneers and foremost authorities in Roentgen-ray work, came to me two years since, with both hands covered with patches of thick epitheliomas and crusted skin, cracked and sore, compelling him to use gloves and cerates for even decent comfort. During several years he had forestalled the dangerous second stage by having surgeons excise and skin graft several parts. Others had cauterized and destroyed certain considerable areas by nitric acid, with fairly smooth scars; several times he had had carbon dioxide freezing to destroy and heal; and other agents as numerous as the surgeons to whom he applied. At last he was disheartened and refused to suffer longer the pain of these treatments, the worst of which he thought was freezing. Two years ago he consulted me and I loaned him one specimen of radium

to use, indicating the number of minutes for each of twenty or thirty places. The result was better, he said, than by any other surgical method he knew. A second use of it on numerous other parts so far restored his hands that he decided to marry, which the condition and prospect of his hands had wholly prevented him from considering. During the past two years he has four times borrowed my specimen to use on a few lingering places, and writes me as follows:"

"The great advantage of the radium treatment, in my judgment, lies, first, in the fact that it may be applied to many situations, which are not accessible to freezing, and, second, in its relative freedom from pain."

"I have had about three hundred and fifty or four hundred areas treated by radium, and about sixty areas treated by freezing. Many of these radium areas could not have been reached successfully by freezing, and because of the relative freedom from pain, it has been possible to obtain truly wonderful results with radium, with far less discomfort than was experienced with the smaller amount of freezing treatments."

"These radium areas included both ulcers and keratoses, most of which could have been classed as precancerous."

"I feel that the success of the radium treatment has really changed my whole life."

"Ten cases of physicians, whose hands, diseased by the Roentgen-ray, I have treated, have all shown the happy results of radium treatment."

"One enthusiastic patient, over 70 years of age, had the usual cure of part of his hand by radium two years after I had excised and skin grafted another area, the microscope having shown typical basal-cell cancer. A third area was then treated by radium at a later date. After the fourth week, he asked me to excise and skin graft the thick scar, as it was on his mind and worried him. It gave a good opportunity for careful microscopic demonstration that no trace of disease was left, but only the subsiding radium inflammation, which would have gone in another fortnight. He remains perfectly well."

"In another surgeon's hands the thick crusted and ulcerated knuckle of his disabled finger has healed after the use of radium, with a soft flexible scar."

"Other surgeons, who were much handicapped in their work, report the same happy termination of their anxiety and pain."

"It seems almost a paradox of radiology that the accepted use of a heavy gamma radiation from a Roentgen tube will cause a diseased condition of the skin, which a similar radiation from a tube of radium will cure. This becomes intelligible when we know that the ouput of the Roentgen-ray tube is almost wholly composed of hard, penetrating, irritating gamma rays. The radium discharges the beta ray in great quantity, as well as the gamma ray. It is the beta ray that has been proved beyond question to be the efficient curative power, and it is only the secondary betas generated by the gamma when striking any resisting substance, that gives it its value in the Roentgen-ray tube work. Hence, we can understand that a surface lesion of morbid cell growth, be it hyperkeratosis or basal cell, is happily cured by the large output of soft beta radiation of radium."

"Regarding the amount of radiant energy needed in such cases, it may be said that, according to what type of radium applicator is

used, the effect which would cure ordinary papillomas or basal cell epithelioma, is competent to cure in equal time, the Roentgen-ray growths. The sequel of an application consists in ten days' latent action, ten days' activity and ten days' quiescence, followed by desquamation of the crusts from a soft healed surface. The results seem permanent. The skin has rarely been found to be irreparably damaged by disease, and afterwards, the cicatrix is thin and flexible."

"To sum up, I may say that no cases have presented themselves to me of chronic dermal Roentgen-ray disease in the early stage of thick patches, cracked, ulcerated and painful, or of epithelial growths of basal-cell type on the back of the left hand, of those who have in past years used that hand to test the tubes, which have not yielded to radium therapy."

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"The Measurement of the Biological Action of X-Rays and Gamma Rays.—Various methods have been employed for measuring the action of X-rays and gamma rays of radium, some of them depending on photographic and chemical, others on electrical and phosphorescent effects. Dr. B. Szilard, however, urges that ionization is the only satisfactory method of measuring the biological action of such rays, although up to the present time it has not been given its proper place in dosage. While there is great physical analogy between the various radiations, it is by no means certain that their biological properties are the same. The fact that dermatitis caused by X-rays has been cured by radium suggests that there are differences in the biological effects of the two forms of radiation. Indeed, such differences might be expected from the fact that gamma rays are perhaps thirty times more penetrating than the hardest X-rays; this quantitative physical difference may readily be translated into a qualitative biological one. The methods of measurement at present in use do not give satisfactory information as to the biological properties of the rays; ionization measures at one, and the same time both the quality and the quantity of the radiant energy. It has the advantages that X-rays are measured after they have left the tube, that it is unaffected by physical factors other than the radiation itself, and that the radiation may be measured in absolute electrical units. The principle of the method is to measure numerically the number of ions liberated under the effect of the radiation, the measurements being carried out by the successive charge and discharge of an electrical condenser of known capacity. The theoretical unit of quantity, which the author proposes, is the amount of radio-active energy necessary to set free a single ion in air, under normal conditions of temperature and pressure. Individual ions, he points out, have an actual existence, determining, as they do, the chemical reactions of a gas, and probably also its biological phenomena, so that the number of ions may really be taken as a measure of the biological effect. For practical purposes, of course, seeing that the energy necessary to set free a single ion is infinitesimal, some multiple of this unit is required, and accordingly he sets up the maga-mega-ion, being the amount of radiation which will set free a million million ions in air; while as corresponding unit of quality he employs the absolute co-efficient of absorption of the rays also in air." Brit. Med. Journ. Feb. 20, 1915, p. 346.

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